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Durability of the EW Sapien Valve and the MDT Core Valve

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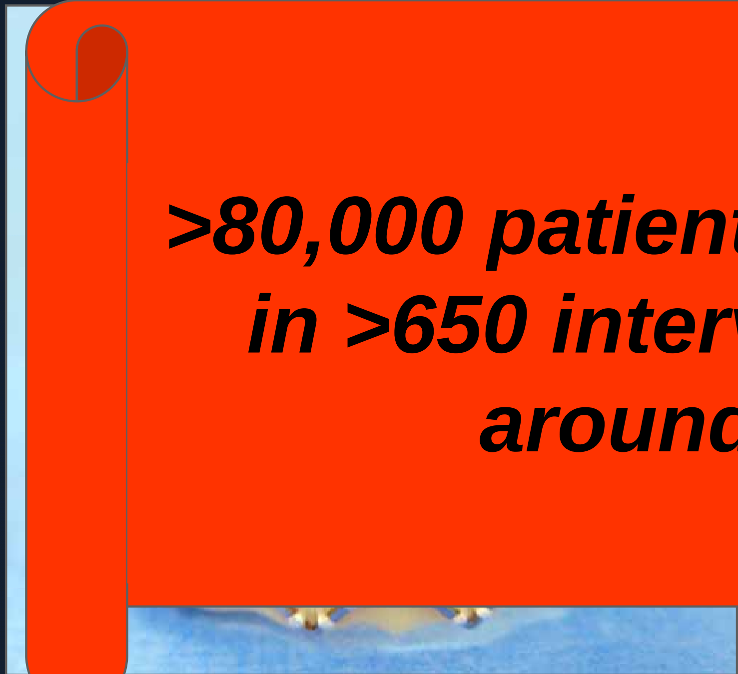
Within the past 12 months, the presenter or their spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Physician Name	Company/Relationship
Eberhard Grube, MD	Medtronic, CoreValve: C, SB, AB, OF Sadra Medical: E, C, SB, AB Direct Flow: C, SB, AB Mitralign: AB, SB, E Boston Scientific: C, SB, AB Biosensors: E, SB, C, AB Cordis: AB Abbott Vascular: AB Capella: SB, C, AB Valtech: E, SB, Claret: SB Keystone Medical: SB

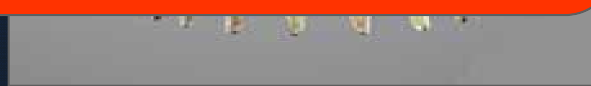
TAVI Arrives

Current Generation Devices

>80,000 patients treated thru 2013 in >650 interventional centers around the globe!



Edwards Lifesciences



Medtronic CoreValve

Anatomic "Footprint" of Edwards Sapien Valve vs. MDT CoreValve

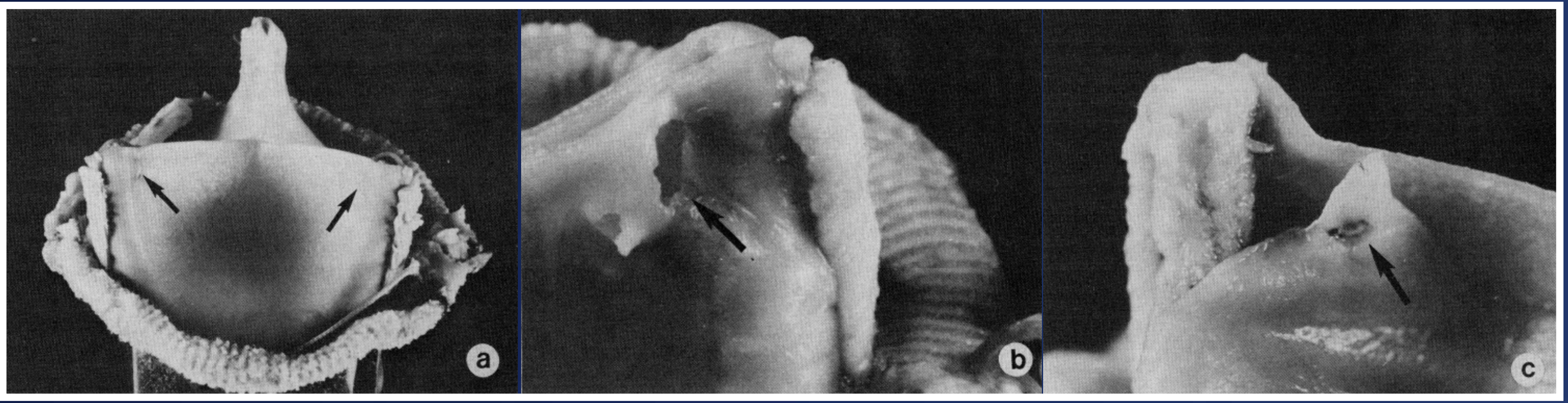
It is not just the "Foot Print" that differentiates Transcatheter Heart Valves

Support structure	Leaflets	Sealing skirt
Nitinol	Bovine pericardium	Porcine pericardium
Stainless steel	Porcine pericardium	Polyester
Cobalt chromium	Porcine aortic valve	Braided polyester
Dacron	± anti-calcification treatment	Polyurethane
		Polyethylene terephalate (PET)

Courtesy of N. Piazza TVT 2013

Valve Durability: A Lesson from Surgical Valves

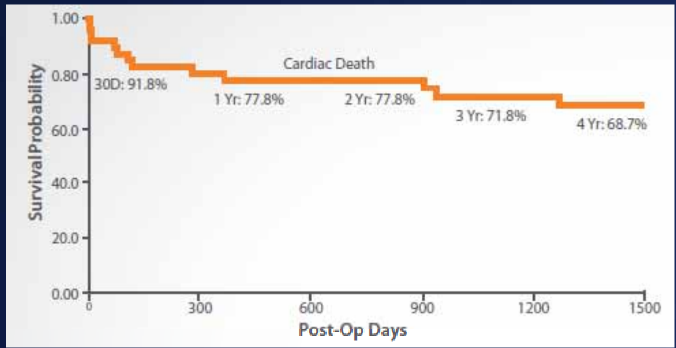
- Long-term survival of bioprosthetic tissue valves requires the minimization of tissue stress and leaflet calcification
  - Leaflet bending/folding during valve operation induces high stresses on leaflets. High bending stresses on leaflets can lead to bending fatigue and potentially delamination, calcification, and/or valve failure[1]
  - Misalignment, leaflet prolapse, asynchrony, poor coaptation, high commissure stress, pinwheeling/bending may lead to early failure.
  - Moderate to severe aortic valve calcification has been identified as an independent predictor of long-term outcomes with impact on both valvular and ventricular function as well as need for reoperation.[2]



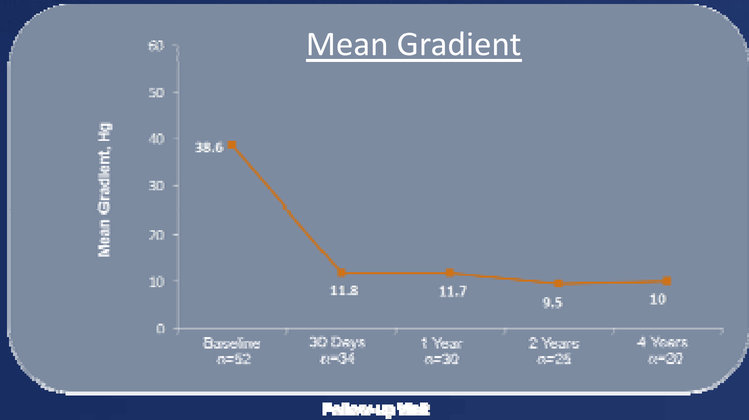
1. *Schoen 1987*
2. Rosenhek R, Binder T, Porenta G, et al. Predictors of outcome in severe, asymptomatic aortic stenosis. *N Engl J Med.* 2000;343:611-17.

The Medtronic CoreValve® System's Durability is demonstrated with Four Year Results.[1]

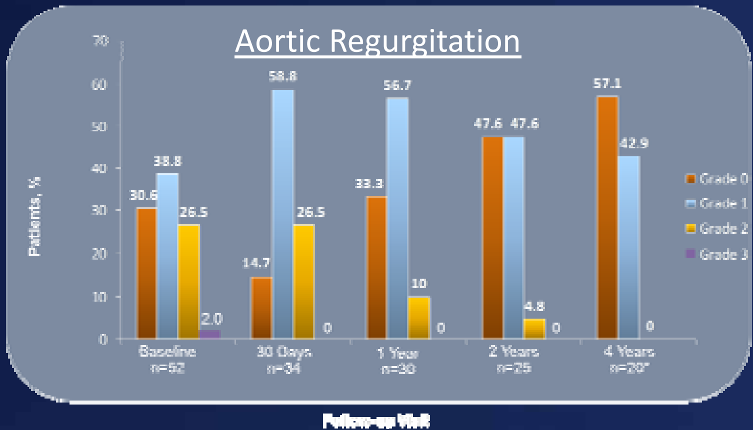
4-year Kaplan-Meier Cardiac Death Survival: 68.0 ± 7.6%[2]



Mean Gradient: 10 mmHg

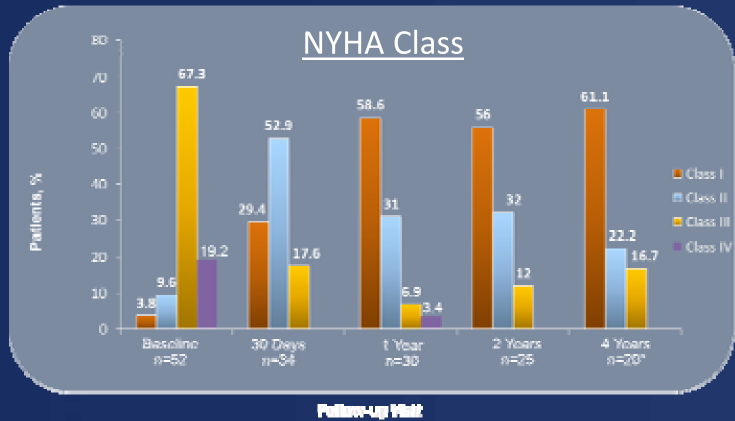


100% patients Grade 0 or Grade 1 AR



*14 of 20 patients were assessed for AR class at 4 years.

83% patients NYHA Class I or II



*18 of 20 patients were assessed for NYHA class at 4 years.

No frame fractures, valve migrations, valve endocarditis, or structural valve deterioration reported at four-years.

1. den Heijer AP et al. "Four year durability and patient survival". Presented at: ESC; Aug 27-31, 2011; Paris, France
2. Medtronic Data on File.

CoreValve® Percutaneous Aortic Valve

Outflow
Orientation

1. **Sits in ascending aorta**
2. **Orientation during deployment**

Constrained Portion
Valve Function

1. **Supra-annular leaflet function**
2. **Designed to avoid coronaries**

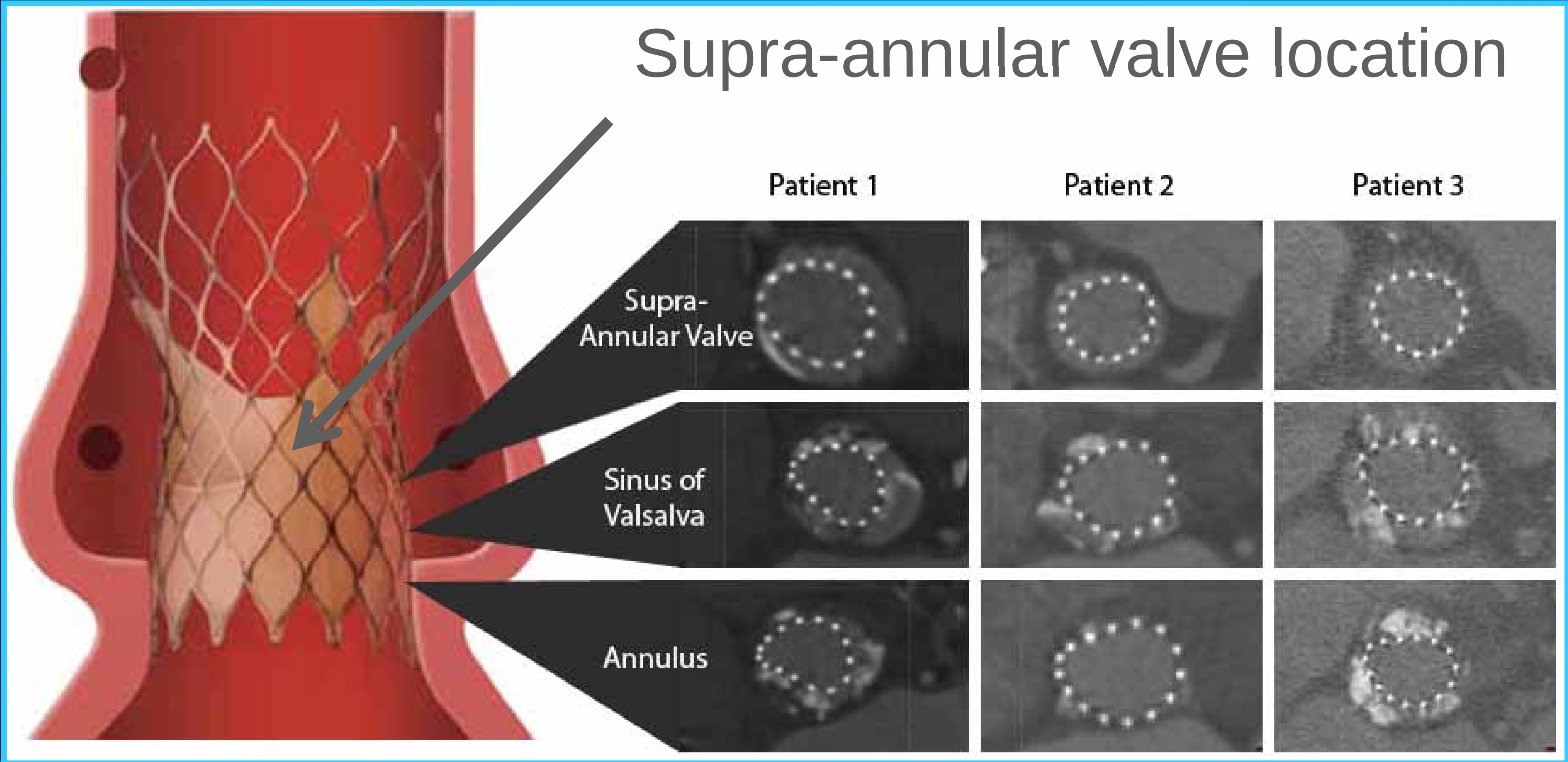
Inflow Portion
Sealing

1. **Intra-annular anchoring**
2. **Mitigates paravalvular aortic regurgitation**

Photograph provided by Piazza, Serruys, and DeJaegere

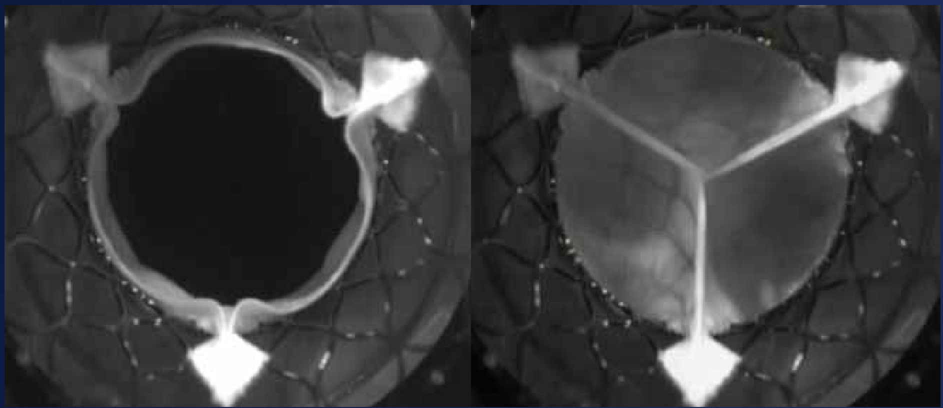
Supra-Annular Valve Design Can Mitigate Impact of Elliptical or Undersized Deployment

- Flexible frame conforms to native annulus shape while maintaining bioprosthesis in a higher position
- Decoupling of valve from native annulus minimizes ellipticity at the valve level

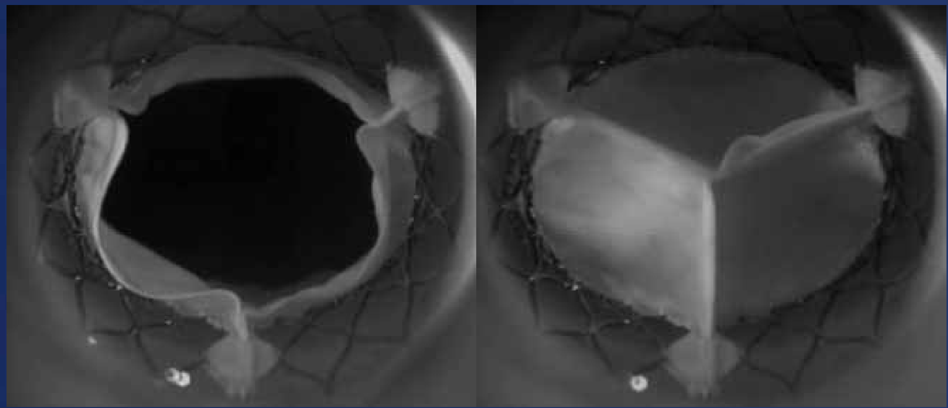


Minimizing Valve Ellipticity Helps Maintain Proper Leaflet Coaptation

- Minimizing valve ellipticity minimizes leaflet prolapsing, buckling, and pinwheeling frequently observed in elliptical valve deployments

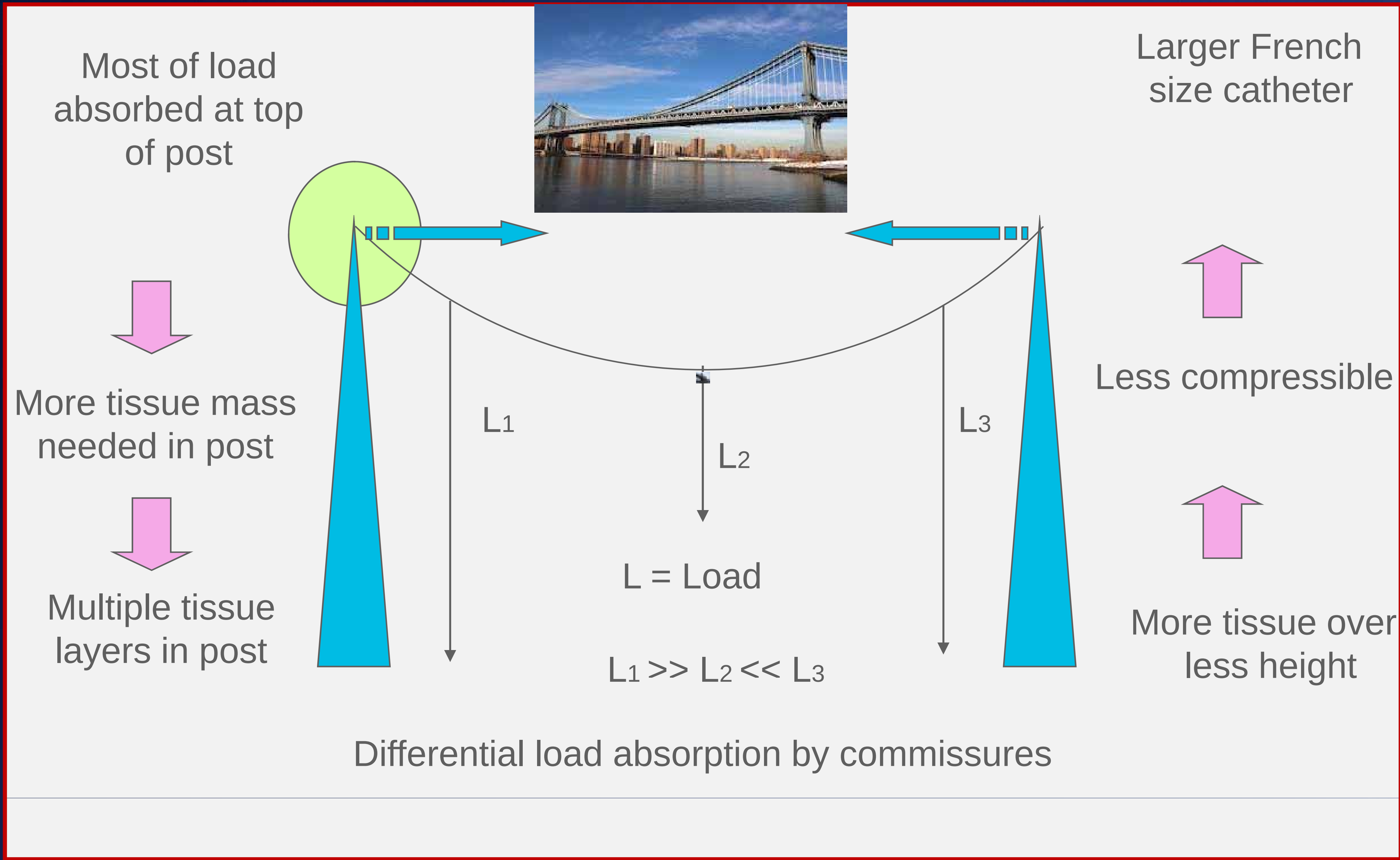


Circular Deployment



Elliptical Deployment
(22mm x 30 mm)

Surgical Bioprosthesis Designs



CoreValve Bioprosthesis Design

Static Frame design

=

Fixed post equivalent

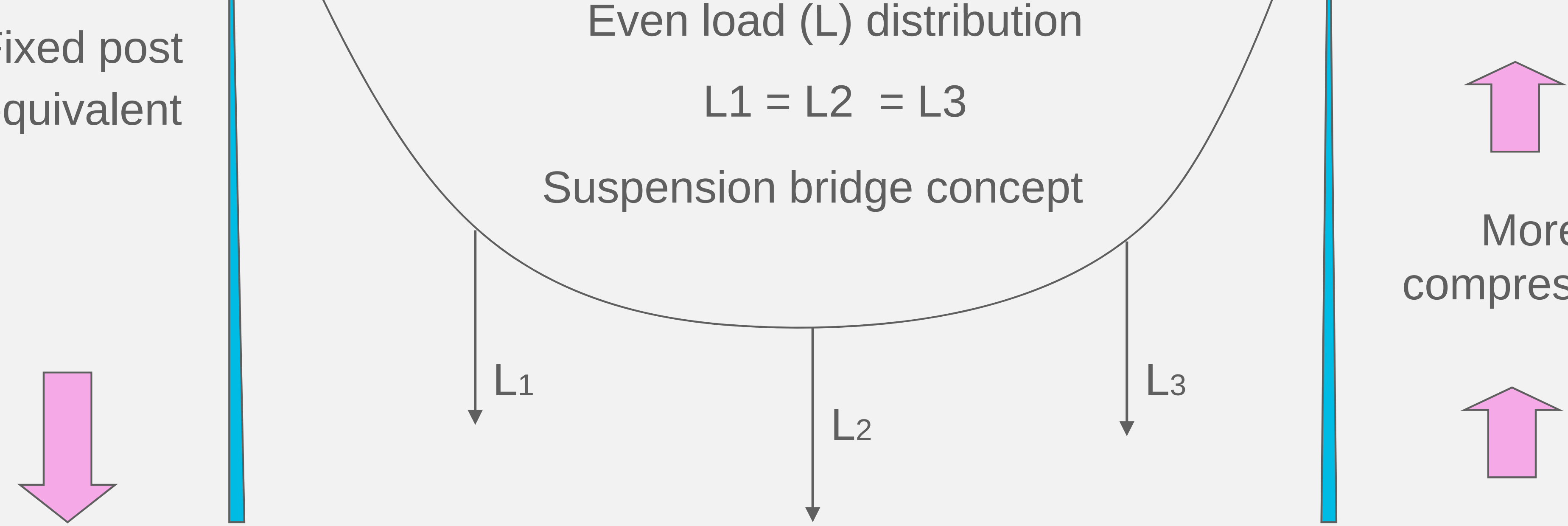
Even load (L) distribution

L1 = L2 = L3

Suspension bridge concept

Smaller French size catheter

More compressible

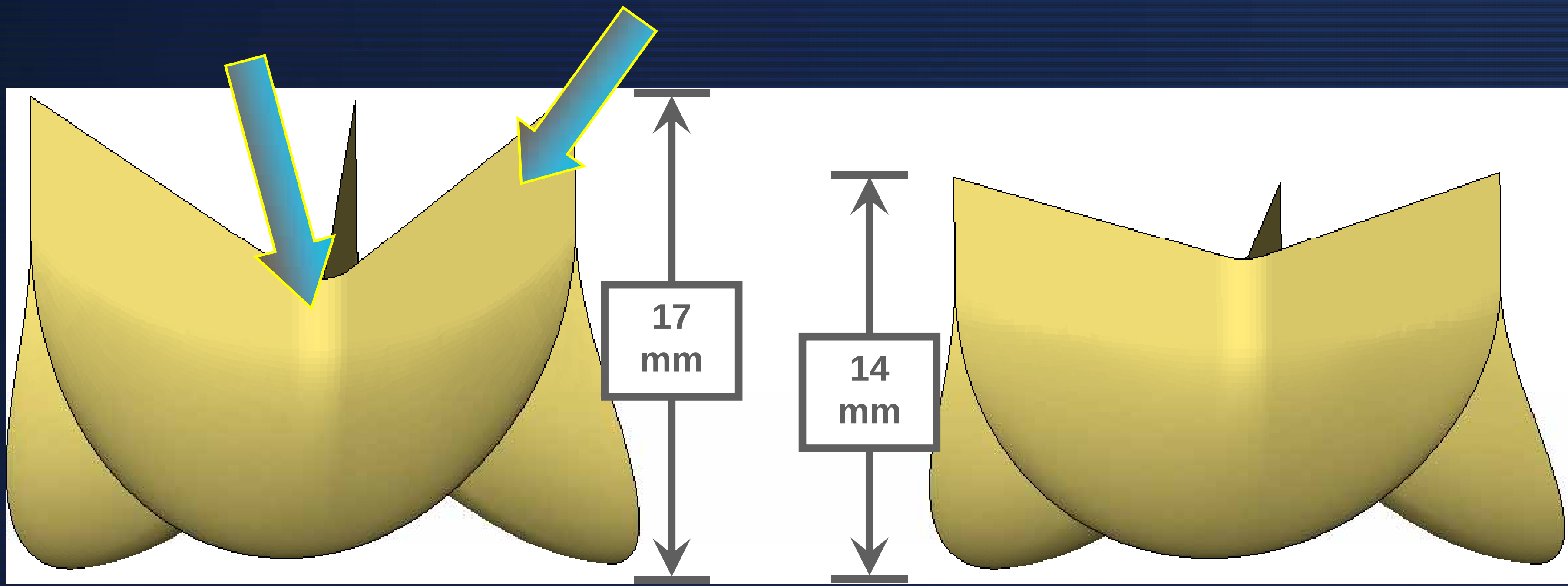


Less tissue mass needed in post area

- Load absorbed equally by each point on leaflet commissures
- NO frame flexing under load

Tissue mass distributed over greater height

CoreValve Leaflet Geometry Incorporates Design Features to Reduce Stresses

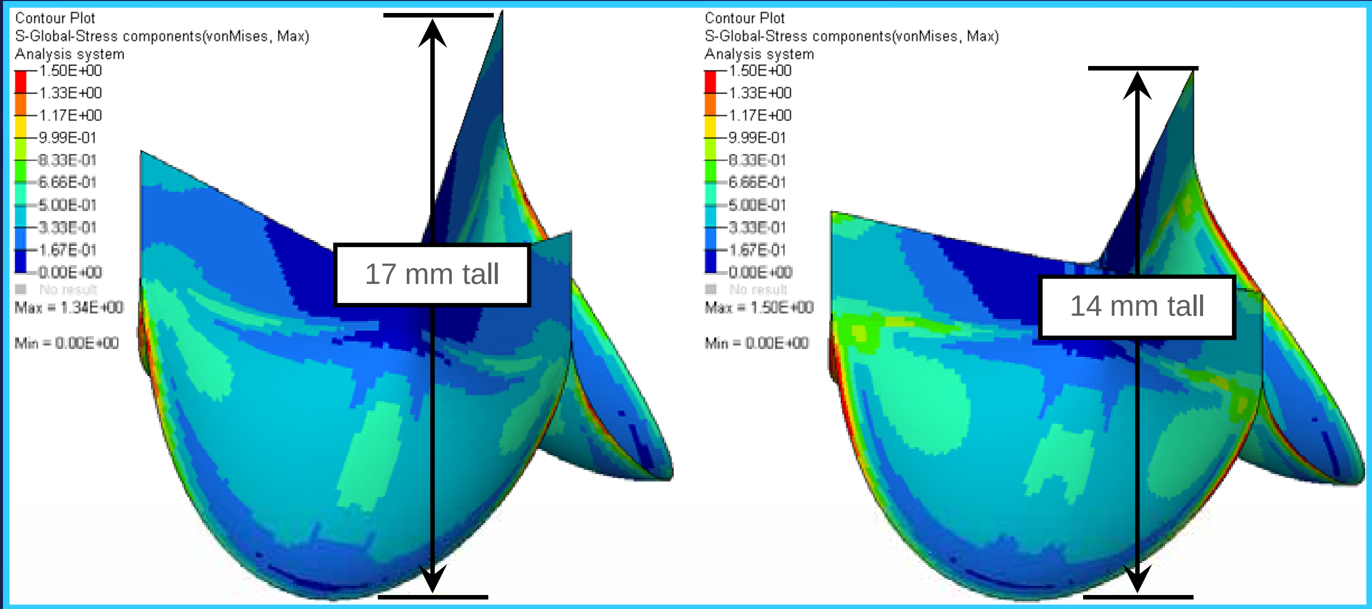


CoreValve Leaflet Design

Traditional Leaflet Design

Commissure height and deep leaflet cuts minimize leaflet stress

- Finite element analysis of the CoreValve® leaflets demonstrate a 12% reduction in stress when compared to traditional valve designs
- Areas of high stress can induce collagen degeneration that over time could lead to tearing and valve failure[1]
- Valve designs that reduce leaflet stresses "are likely to have improved performance in long-term applications"[2]

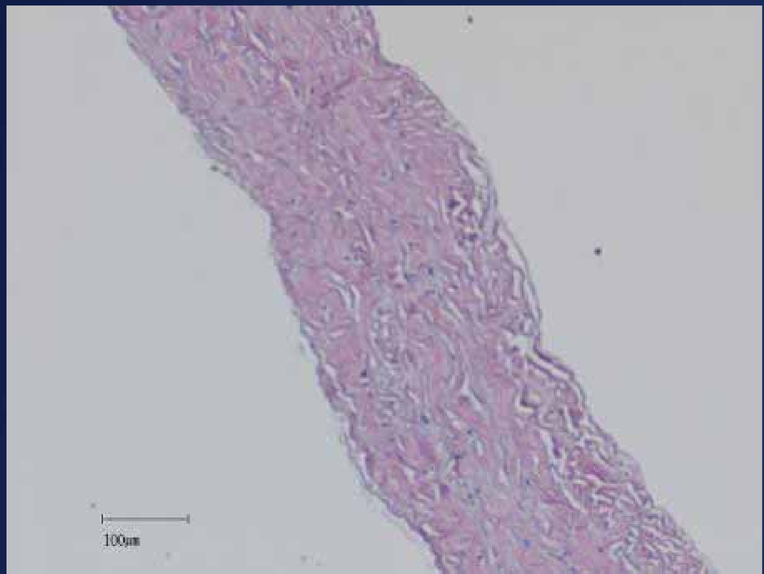


Max Stress = 1.34 MPa **Max Stress = 1.50 MPa**

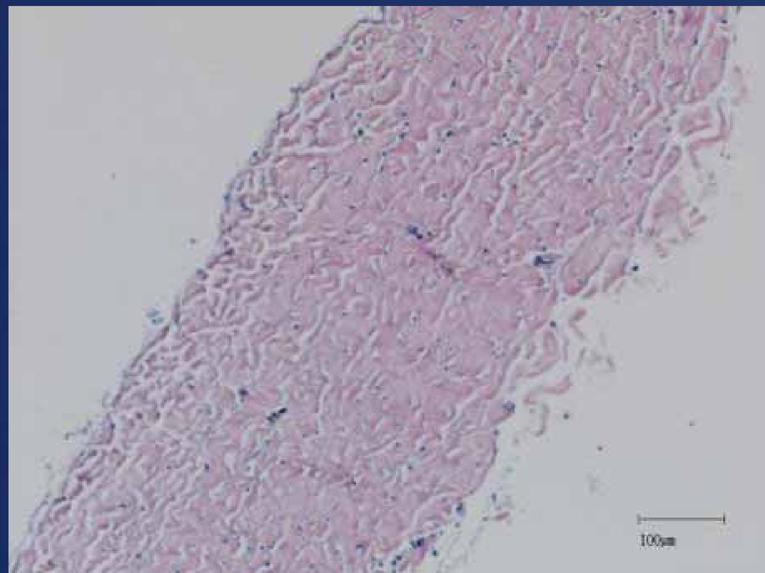
1. Schoen Frederick J. Cardiac Valve Prostheses: Pathological and Bioengineering Considerations. *J Cardiac Surg*. 1987;2:65-108.
2. Sun W., Li K., Sirois E. Simulated elliptical bioprosthetic valve deformation: Implications for asymmetric transcatheter valve deployment. *J Biomech*. 2010;43:3085-3090.

Porcine Pericardium Thickness is Well Suited for Transcatheter Valve Delivery

- Thin tissue enables minimized delivery catheter size
- Porcine pericardium thickness is about half that of bovine despite being very structurally similar[1,2]
- Both composed of randomly oriented collagen bundles



Porcine



Bovine

1. Sacks MS. Uniaxial mechanical and structural properties of bovine versus porcine pericardial tissue. Medtronic Engineered Tissue Mechanics Laboratory. University of Pittsburgh, Pittsburgh, PA. January 17, 2008. Data on File.

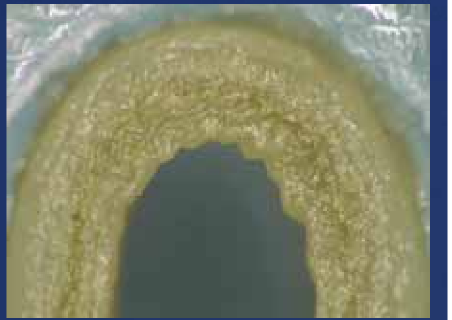
2. Braga-Vilela AS, Pimentel ER, Marangoni S, Toyama MH, de Campos Vidal B. Extracellular matrix of porcine pericardium: Biochemistry and collagen architecture. *J Membr Biol.* 2008 Jan;221(1):15-25.

Porcine pericardium is the optimal tissue for valve performance and low-profile delivery

Thin

Porcine pericardium thickness is about half that of bovine. Thinner tissue prevents tissue damage during crimping, tracking, and deployment, allowing for low-profile delivery across all valve sizes.[1,2]

Porcine Pericardium

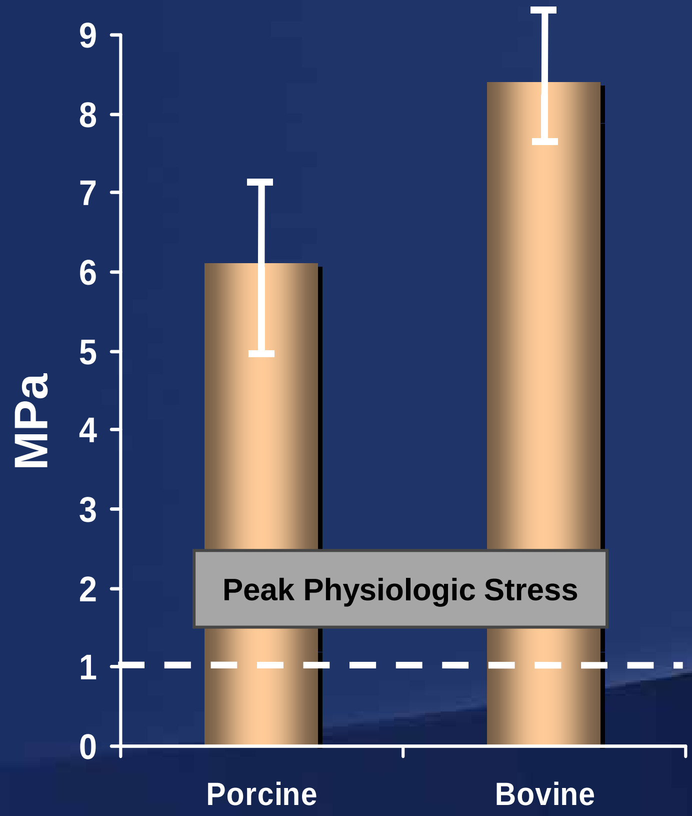


Bovine Pericardium

Magnification 175X

Strong

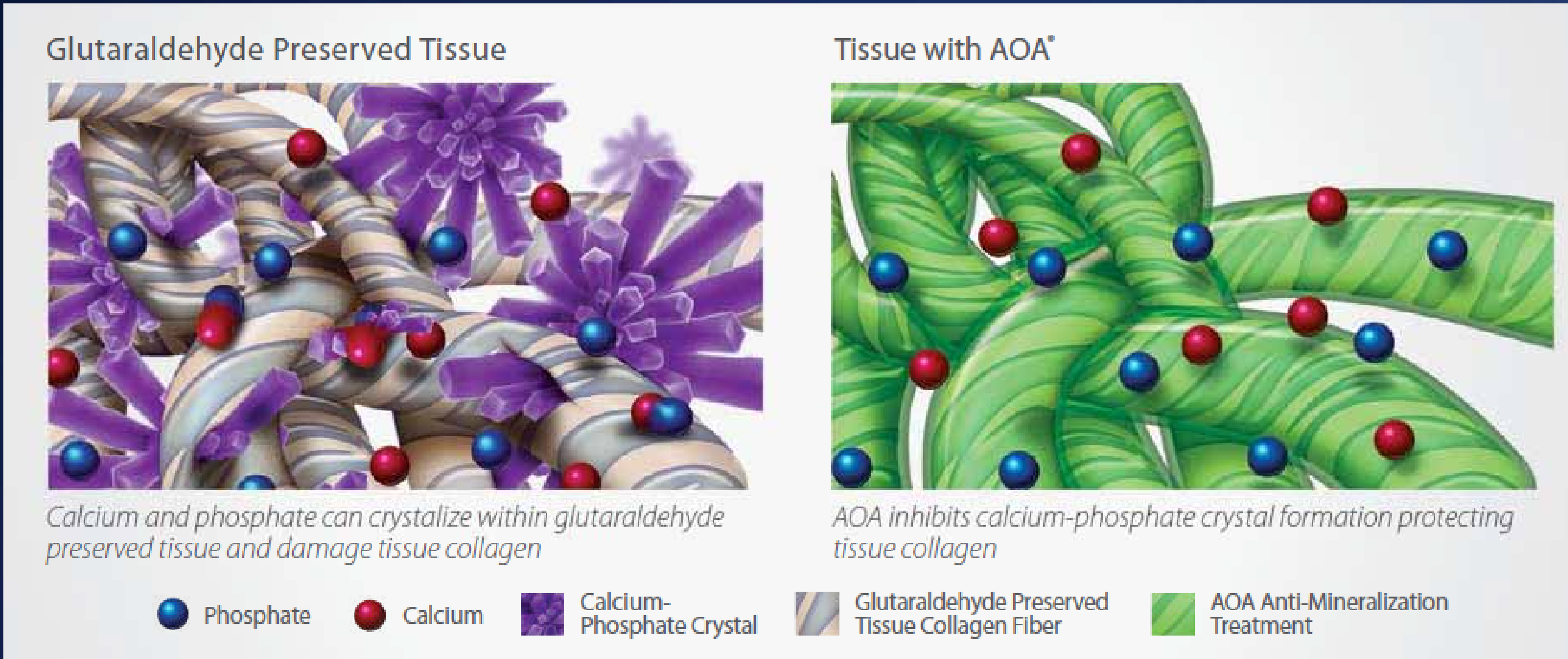
The ultimate tensile strength (UTS) and suture pull out stresses for porcine and bovine pericardium are statistically equivalent[1,3] and peak physiologic stresses are significantly less than both UTS values[4]



1. Sacks MS. Uniaxial mechanical and structural properties of bovine versus porcine pericardial tissue. Medtronic Engineered Tissue Mechanics Laboratory. University of Pittsburgh, Pittsburgh, PA. January 17, 2008. Data on File.
2. Braga-Vilela AS, Pimentel ER, Marangoni S, Toyama MH, de Campos Vidal B. Extracellular matrix of porcine pericardium: Biochemistry and collagen architecture. *J Membr Biol*. 2008 Jan;221(1):15-25.
3. Garcia Paez JM, Carrera A, Herrero EJ, et al. Influence of the selection of the suture material on the mechanical behavior of a biomaterial to be employed in the construction of implants. Part 2: porcine pericardium. *J Biomater Appl*. 2001;16:68-90.
4. Li, K and Sun, W. "Simulated thin pericardial bioprosthetic valve leaflet deformation under static pressure-only loading conditions: Implications for percutaneous valves" *Ann Biomed Eng*. 2010 Aug;38(8):2690-701.

AOA® anti-mineralization treatment reduces both early and late valvular calcification

- Alpha-amino oleic acid (AOA®) treatment inhibits calcium formation on prosthetic valve leaflets.
- Unlike surfactants, AOA bonds with the tissue to block calcium binding.
- AOA has 20 years of proven clinical success on Medtronic's surgical valves.[1]



Conclusion (Core Valve)

- Long-term survival of bioprosthetic tissue valves requires the minimization of tissue stress and leaflet calcification
- CoreValve's design and tissue selection are intended to ensure durability and long-term performance.
- The Medtronic CoreValve® System's Durability is Demonstrated with with no frame fractures, valve migrations, valve endocarditis, or structural valve deterioration reported at four-years.
- The ADVANCE study demonstrates CoreValve's EOA and mean gradient remain stable over time

Edwards TAVR System: Design, Development and Clinical Results

Four Principles of AVR Remain Unchanged

Principles	sAVR
Predictable Procedure	• Implantability
Optimal Hemodynamics	• Circular frame design, optimal leaflet opening
Low Rate of Complications	• Low thrombogenicity, low PVL, low conduction disturbances, low bleeding
Durability	• Circular geometry for low leaflet stress • Tissue choice • Anti-calcification tissue treatment

1. Harken DF, et al. Aortic valve replacement with a caged ball valve. *Am J Cardiol* 1962; 9:292-299.

The 4 Principles of Aortic Valve Design apply to future transcatheter Heart Valves

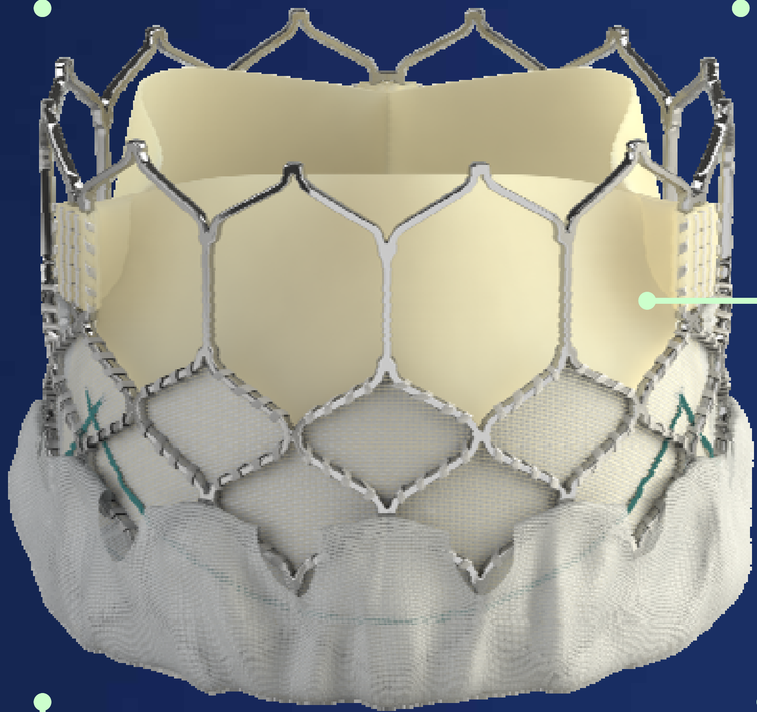
Principles	Edwards SAPIEN 3 THV	Edwards CENTERA System
Predictable procedure	• Balloon-expandable design • Fine control of valve positioning and deployment	• Motorized delivery with touch deployment
Optimal hemodynamics	• Circular expansion at the annulus	• Contoured frame design for optimal seating
Low rate of complications	• Outer skirt and high radial strength frame minimize PV leak • Low frame height	• Contoured frame design for sealing in the annulus • Low frame height
Durability	• Circular expansion at leaflet level • Bovine pericardial tissue • Anti-calcification treatment and leaflet matching	• Bovine pericardial tissue • Anti-calcification treatment and leaflet matching
	Next-generation, balloon-expandable platform: most closely aligned with optimal AVR principles	**Controlled-release** nitinol-frame technology: aligns more closely with principles of nitinol valves

SAPIEN 3: Designed for TAVI as Intended – Low Complications, High Performance

Enhanced frame design

- New frame geometry allows 14F profile
- High radial strength providing circularity for optimal hemodynamics and durability

Low frame height
for low conduction disturbance



Bovine pericardial tissue

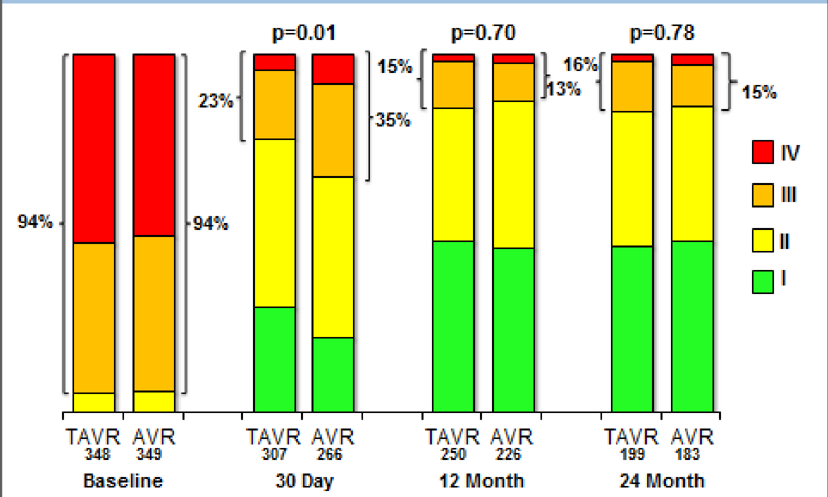
- Optimized leaflet shape and tissue treatment for durability

New outer skirt
PV leak solution

Both AVR and TAVR are Highly Effective

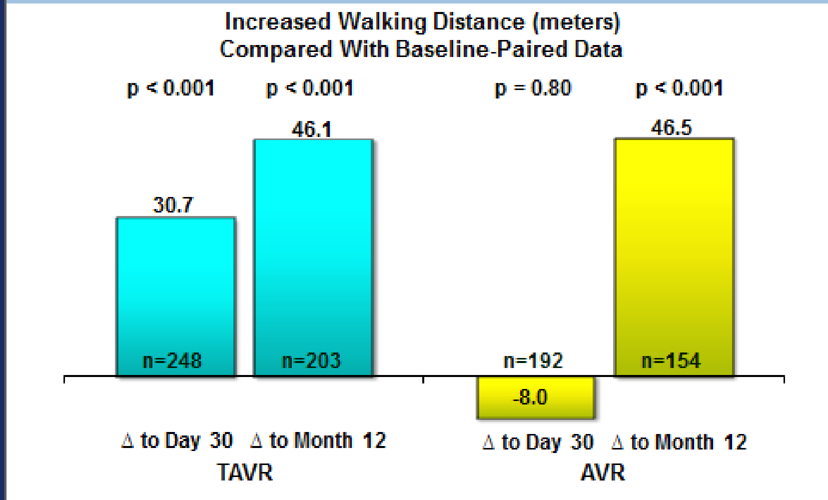
NYHA Class Over Time Survivor Analysis

(ITT Population)



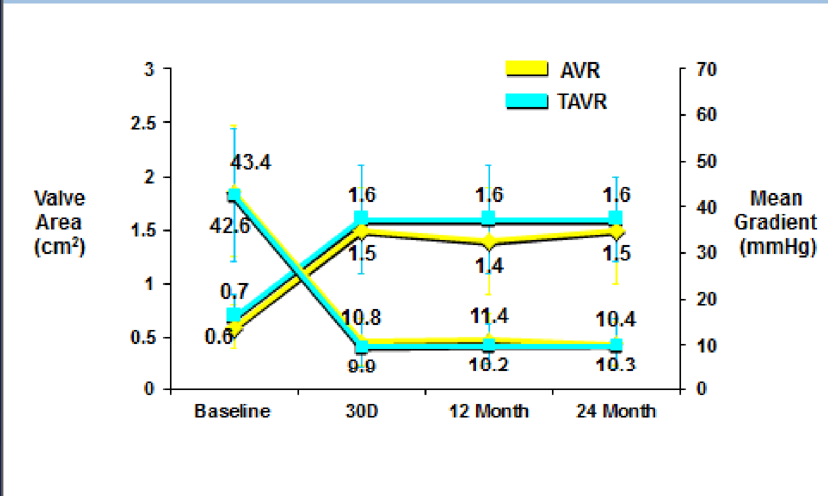
Six-Minute Walk Tests

(ITT Population)

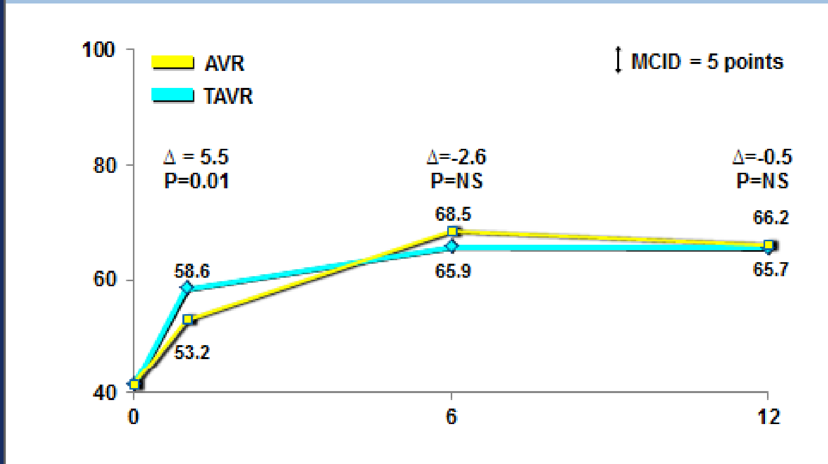


Echocardiography Assessments AV Areas

(AT Population)



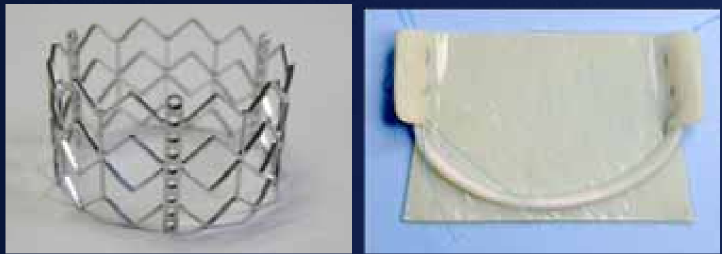
Primary Endpoint KCCQ Overall Summary



Growth curve analysis; adjusted for baseline MCID = minimum clinically important difference

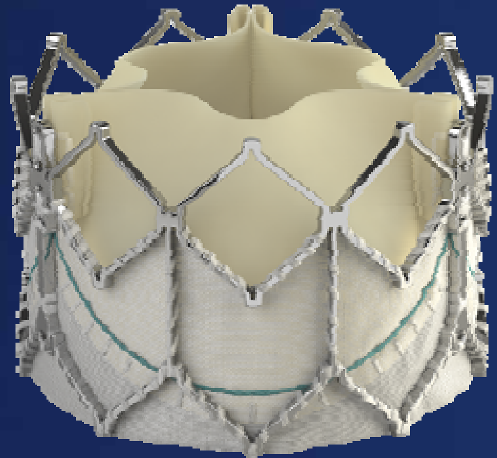
Transcatheter Valve Program:
Grounded in Over 50 Years of Valve Expertise

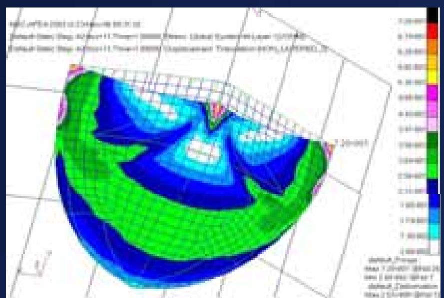
DESIGN



Frame & Leaflet Geometry

Tissue Attachment





Finite Element Analysis

- Laser Cutting
- Heat Treatment
- Electro Polishing
- Materials selection
- Tissue Treatment
- Hemodynamics
- Fatigue

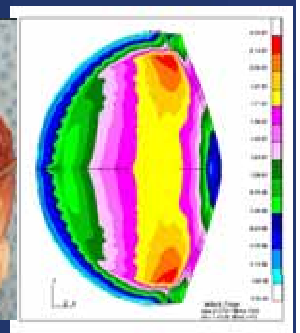
TESTING

AWT

Pulsatile Flow

- Raw Materials
- Calcification
- Fatigue
- Expansion
- Recoil
- Corrosion
- MRI

Animal Models

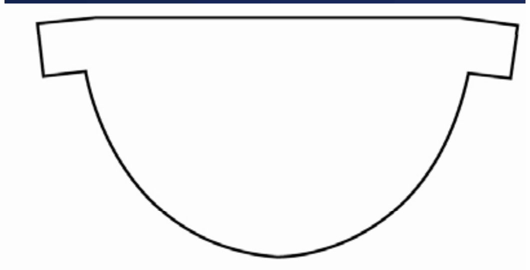


FEA

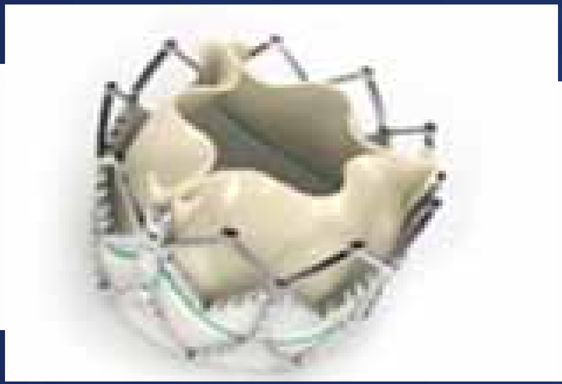
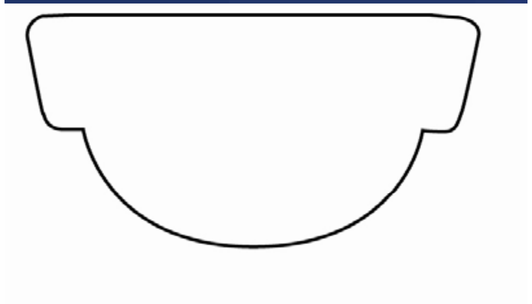
Leaflet Design Considerations

Leaflet design and manufacturing based on Edwards clinically proven surgical aortic tissue valves

- Proven bovine pericardial tissue
- Proprietary surgically-shaped leaflets
- Leaflet matching process for thickness and elasticity
- ThermaFix anti-calcification technology

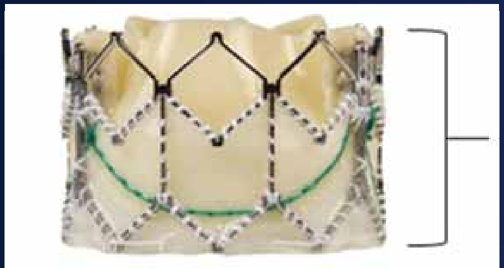
Edwards surgical heart valve

Edwards SAPIEN XT

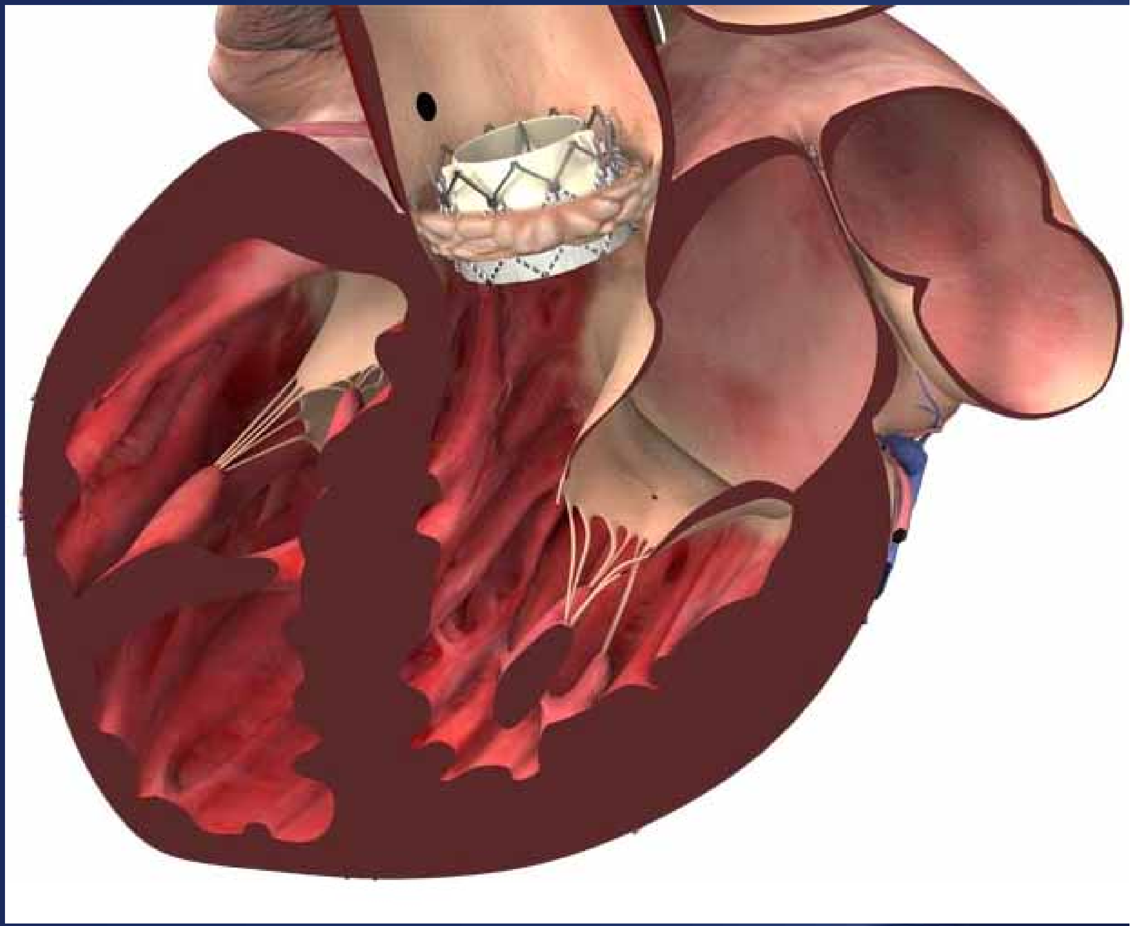
Optimized Frame Height

The Edwards SAPIEN XT frame is optimized for proper placement and non-interference with the surrounding anatomy



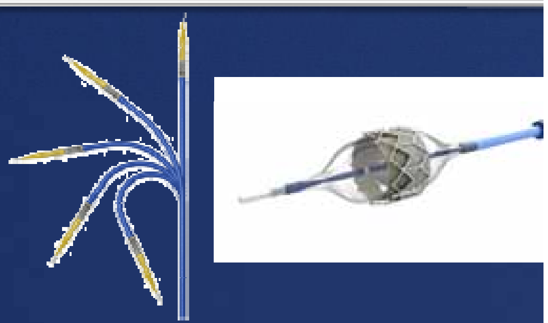
14 – 19mm

Valve Size	SAPIEN Valve Height	SAPIEN XT Valve Height
20 mm		14 mm
23 mm	14 mm	14 mm
26 mm	16 mm	17 mm
29 mm		19 mm



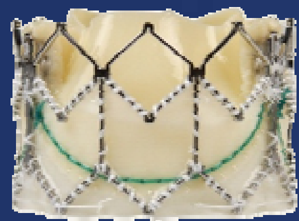
Core Principles of Edwards Transcatheter Valve Technology

Reliable Delivery
Balloon expandable for accurate valve placement and deployment



Circular at the Annulus and Leaflet Level
Balloon-expandable to open round plus high radial strength frame design to maintain proper shape for hemodynamics and durability

Low Frame Height
Frame height optimized for proper placement and non-interference with the surrounding anatomy minimizing complications



Durable Leaflet Design
Technologically advanced leaflet design and manufacturing based on Edwards clinically proven aortic tissue valves

Conclusion (Edwards)

- The last 5 years has spawned not only an explosion of global clinical experience with TAVI, but unprecedented clinical science to rapidly advance the field

- Third and future generation platforms designed to broaden populations and optimize outcomes